

Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (Currently Amended) A multiple inducible gene regulation system consisting of two orthogonal gene regulation systems, wherein:

a) each of said orthogonal gene regulation systems comprises:

i) a polynucleotide encoding a receptor complex comprising:

A) a DNA binding domain;

B) a ~~Group H nuclear~~ an ecdysone receptor ligand binding domain and a nuclear receptor ligand binding domain capable of forming a dimer with the ~~Group H nuclear~~ ecdysone receptor ligand binding domain; and

C) a transactivation domain; and

ii) a polynucleotide comprising a DNA sequence encoding a polypeptide operatively linked to a response element,

wherein binding of the DNA binding domain to the response element results in expression of the polypeptide.

2. (Currently Amended) The multiple inducible gene regulation system of claim 1, wherein each operable gene regulation system comprises

a) i) a first gene expression cassette comprising a polynucleotide that encodes a

polypeptide comprising a transactivation domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a ~~Group I nuclear~~ an ecdysone receptor ligand binding domain, and

ii) a second gene expression cassette comprising:

A) a response element recognized by the DNA-binding domain;

B) a promoter that is activated by the transactivation domain; and

C) a gene whose expression is to be modulated;

b) i) a first gene expression cassette comprising a polynucleotide that encodes a polypeptide comprising a transactivation domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a ~~Group I nuclear~~ an ecdysone receptor ligand binding domain,

ii) a nuclear receptor ligand binding domain selected from the group consisting of a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, an ultraspiracle protein ligand binding domain, and a chimeric ligand binding domain comprising two polypeptide fragments, wherein the first polypeptide fragment is from a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate retinoid X receptor ligand binding domain, or ultraspiracle protein ligand binding domain, and

iii) a second gene expression cassette comprising:

A) a response element recognized by the DNA-binding domain;

B) a promoter that is activated by the transactivation domain; and

- C) a gene whose expression is to be modulated; or
- c) i) a first gene expression cassette comprising a polynucleotide that encodes a first polypeptide comprising a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated and a ~~Group H nuclear~~ an ecdysone receptor ligand binding domain,
- ii) a second gene expression cassette comprising a polynucleotide that encodes a second polypeptide comprising a transactivation domain and a ~~Group H nuclear~~ an ecdysone receptor ligand binding domain, and
- iii) a third gene expression cassette comprising:
- A) a response element recognized by the DNA-binding domain;
- B) a promoter that is activated by the transactivation domain; and
- C) a gene whose expression is to be modulated.
3. (Original) A virus comprising the multiple gene regulation system of claim 1.
4. (Previously Presented) An isolated cell comprising the multiple gene regulation system of claim 1.
5. (Canceled)
6. (Canceled)

7. (Previously Presented) The multiple inducible gene regulation system of claim 1, wherein said receptor complex is a non-mammalian receptor complex.

8. (Canceled)

9. (Currently Amended) A multiple inducible gene regulation system consisting of two orthogonal gene regulation systems wherein:

a) each of said gene regulation systems comprises:

i) a receptor complex comprising:

A) a DNA binding domain;

B) ~~a Group H nuclear~~ an ecdysone receptor ligand binding domain and a nuclear receptor ligand binding domain capable of forming a dimer with the ~~Group H nuclear~~ ecdysone receptor ligand binding domain; and

C) a transactivation domain; and

ii) a polynucleotide comprising:

an exogenous or endogenous gene and a response element;

wherein:

A) the exogenous or endogenous gene is under the control of the response element;

and

B) binding of the DNA binding domain to the response element in the presence of a ligand results in activation of the gene.

10. (Currently Amended) The multiple inducible gene regulation system of claim 9, wherein each operable gene regulation system comprises:

- a) i) a polypeptide comprising a transactivations domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a ~~Group H nuclear~~ an ecdysone receptor ligand binding domain, and
 - ii) a gene expression cassette comprising:
 - A) a response element recognized by the DNA-binding domain of the polypeptide of a)i);
 - B) a promoter that is activated by the transactivation domain of the polypeptide of a)i); and
 - C) a gene whose expression is to be modulated;
- b) i) a polypeptide comprising a transactivation domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a ~~Group H nuclear~~ an ecdysone receptor ligand binding domain,
 - ii) a nuclear receptor ligand binding domain selected from the group consisting of a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, an ultraspiracle protein ligand binding domain, and a chimeric ligand binding domain comprising two polypeptide fragments, wherein the first polypeptide fragment is from a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate retinoid X receptor ligand binding domain, or ultraspiracle protein ligand binding domain, and

iii) a gene expression cassette comprising:

A) a response element recognized by the DNA-binding domain of the polypeptide of b)i);

B) a promoter that is activated by the transactivation domain of the polypeptide of b)i); and

C) a gene whose expression is to be modulated; or

c) i) a first polypeptide comprising a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated and a ~~Group H nuclear~~ ecdysone receptor ligand binding domain,

ii) a second polypeptide comprising a transactivation domain and a nuclear steroid receptor ligand binding domain, and

iii) a gene expression cassette comprising:

A) a response element recognized by the DNA-binding domain of the first polypeptide of c)i);

B) a promoter that is activated by the transactivation domain of the second polypeptide of c)ii); and

C) a gene whose expression is to be modulated.

11. (Canceled)

12. (Previously Presented) An isolated cell comprising the multiple gene regulation system of claim 9.

13. - 49. (Canceled)

50. (New) A vector comprising the multiple inducible gene regulation system of claim 1.

51. (New) The isolated host cell of claim 4, wherein the host cell is a bacterial cell, a fungal cell, a yeast cell, a plant cell, an animal cell, a mammalian cell, a mouse cell, or a human cell.

52. (New) The isolated host cell of claim 51, wherein the host cell is a human cell.

53. (New) The isolated host cell of claim 12, wherein the host cell is a bacterial cell, a fungal cell, a yeast cell, a plant cell, an animal cell, a mammalian cell, a mouse cell, or a human cell.

54. (New) The isolated host cell of claim 53, wherein the host cell is a human cell.